CT-guided transthoracic fine needle aspiration of pulmonary lesions: Accuracy and complications in 134 cases

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ÖZET

Akciğer lezyonlarında BT eşliğinde transtorasik ince iğne aspirasyonu: 134 olguda etkinlik ve komplikasyonlar

Bu prospektif çalışmanın amacı; akciğer lezyonlarının tanısında bilgisayarlı tomografi (BT) eşliğinde transtorasik ince iğne aspirasyonu (TTİİA)'nun etkinliğini değerlendirmek ve bu prosedürün komplikasyon oranını tespit etmektir. Aralık 2003-Ağustos 2005 tarihleri arasında merkezimizde BT eşliğinde TTİİA yapılan 134 olgu prospektif olarak değerlendirildi. Tüm ince iğne aspirasyonları 22-gauge Chiba iğnesi ile BT eşliğinde yapıldı. Biyopsilerin hepsi tek göğüs hastalıkları uzmanı tarafından yapıldı. Çalışmamızdaki olguların 122 (%91)'si kötü huylu, 12 (%9)'si iyi huylu lezyon tanısı aldı. Kötü huylu 122 lezyonun 107 (%88)'sine doğru teşhis kondu ve iyi huylu lezyonların %42'sinde spesifik tanı elde edildi. Malignite tanısında TTİİA'nın sensitivitesi %83, etkinliği %84 idi. Yüz otuz dört olgunun 22 (%16)'sinde pnömotoraks gelişti. Pnömotoraks santral lokalizasyonlu lezyonlarda daha sık görüldü (p= 0.001). Sonuçlarımız; BT eşliğinde TTİİA'nın yüksek tanısal etkinliğe ve kabul edilebilir komplikasyon oranlarına sahip olduğunu düşündürmektedir. Ayrıca, pnömotoraks riskini artıran en önemli faktörün, örneklem için geçilen havalı alan derinliğinin artışı olduğunu düşünmekteyiz.

Anahtar Kelimeler: *İnce iğne aspirasyonu, transtorasik, bilgisayarlı tomografi, akciğer kanseri.*

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SUMMARY

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The aim of this study was to perform a prospective evaluation of the effectiveness of computed tomography (CT)-guided transthoracic fine needle aspiration (TFNA) in the diagnosis of pulmonary lesions and to determine the complication rate of this procedure. A prospective review was conducted of 134 patients who underwent CT-guided TFNA at our center between December 2003 and August 2005. All fine needle aspirations were performed with a 22-gauge single-pass Chiba needle under CT guidance. The biopsies were performed by one pulmonologist. Two hundred twenty two (91%) malignant lesions and 12 (9%) benign lesions were reviewed in the present study. An accurate diagnosis was made in 107 (88%) of the 122 malignant lung lesions and a specific diagnosis was obtained in 42% of the benign lesions. The sensitivity of TFNAs for the detection of malignancy was 83%, and the overall accuracy of TFNA for diagnosing malignancy was 84%. Pneumothorax occurred in 22 of the 134 patients (16%). Pneumothorax was more frequently observed in centrally located lesions (p= 0.001). Our results suggest that CT-guided TFNA has a high diagnostic accuracy and an acceptable rate of complications. Moreover, we suggest that the most important factor increasing the risk of pneumothorax is an increase in the depth of aerated lung traversed for sampling.

Key Words: *Fine-needle aspiration, transthoracic, computed tomography, lung cancer.*

Transthoracic fine needle aspiration (TFNA) is widely viewed as a reliable diagnostic technique for pulmonary nodules and masses. It is a powerful diagnostic tool, especially for malignant pulmonary lesions. Despite its success with malignant lesions, however, it has a low diagnostic accuracy for benign lesions.

TFNA can be performed under the guidance of fluoroscopy, ultrasound, and computerized tomography (CT). Studies have reported that the diagnostic sensitivity of TFNA with fluoroscopy is higher than that of TFNA with CT (1). Ultrasound-guided TFNA is the most reliable, fastest, and cheapest method with lesions fixed to the chest wall (2). The most important advantage of CT guidance is its applicability to lesions of every size and location (3).

The most common complication of TFNA biopsy is pneumothorax, and less frequently, parenchymal hemorrhage and hemoptysis occur. Air embolus is rare but very serious (4).

The aim of this study was to perform a prospective evaluation of the effectiveness of CT-guided TFNA in the diagnosis of pulmonary lesions and to determine the complication rates of this procedure.

MATERIALS and METHODS

We prospectively evaluated the cases of 134 patients who underwent CT-guided TFNA in our clinic between December 2003 and August 2005. The patients in 120 (90%) of the 134 cases were men [14 subjects (10%) were women].

Before the TFNA, all patients underwent chest radiography, CT, and routine laboratory testing. Additionally, all patients passed coagulation tests, and hemocoagulation parameters in all patients were found to be within normal limits. Respiratory function tests were performed in those

with chronic obstructive pulmonary diseases. The lung fields were subdivided into peripheral and central with respect to lesion location. The central zone included any lung lesion with a center that fell within a 4 cm radius of the hilum (5).

The biopsies were performed by a single pulmonologist who had 5 years of experience with this procedure. All biopsies were performed according to a standard protocol. Informed consent was obtained from all patients before the procedure. Patients were placed in either the prone or supine position, depending on the location of the lesion. When choosing an approach for the biopsy, the maximum effort was made to traverse the least possible amount of aerated lung to avoid crossing bullae and vascular structures and minimize the number of pleural surfaces crossed by the aspiration needle. At the time of biopsy, CT images were obtained at a 5 mm section thickness throughout the lesion. Localization was determined by CT imaging with laser lights and markers on the skin. The needle entry site was prepared and draped with a povidone-iodine solution, and a 1% lidocaine solution was used for local anesthesia. The TFNA was performed with a 22-gauge single pass Chiba needle that was 9 or 15 cm in length. A 20 mL syringe was used to aspirate the material. Because a cytopathologist was not present during lesion sampling, pathology slides were prepared by the operating physician at the time of aspiration and fixed immediately in 95% alcohol. The specimens were transferred to the pathology department for analysis. If infection was suspected, a Gram stain, an acid-fast stain, and cultures were performed. Biopsy specimens were defined as positive for malignancy, definitively benign, or non-specific. In patients with nonspecific TFNA biopsies, the TFNA procedure was repeated if a medium or high likelihood of malignancy was suspected. If the likelihood of malignancy was low and the diagnosis was clinically and radiologically benign, the TFNA procedure was not repeated.

The patient was monitored after the procedure for complications for 4 hour. Chest radiographs were obtained within 1 h after the procedure to determine whether a pneumothorax had occurred. Any patients who developed a pneumothorax were followed up in the hospital.

For statistical analysis, each case with a final diagnosis was classified as either malignant or benign. Final malignant diagnoses were based on the pathologic evaluation of surgically resected specimens, definitive diagnosis of malignancy at TFNA, the results of biopsies of other sites, and the occurrence of a clinical course that was consistent with cancer. Final benign diagnoses were based on the pathologic evaluation of surgically resected specimens and the observation on clinical and radiological follow-up that the lesion had remained stable (4,6-8).

We used chi-square and Mann-Whitney U tests to assess the significance of our findings, with $p < 0.05$ considered statistically significant.

RESULTS

General Considerations

The subjects consisted of 120 (90%) men and 14 (10%) women. The mean age was 58.9 ± 11.6 years (range 17-82 years). A hundred and eleven (83%) subjects were active smokers, 14 (10%) were nonsmokers, and 9 (7%) were former smokers. The mean cigarette history was 51.2 ± 30.7 pack years.

We found that the lesions were in the right lung in 76 (57%) cases, the left lung in 52 (39%) cases, the hilum in 2 (1%) cases, the mediastinum in 3 (2%) cases, and the chest wall in the other cases. The 76 lesions in the right lung were positioned as follows: 52 (68%) in the upper lobe, 8 (11%) in the middle lobe, and 16 (21%) in the lower lobe. The 52 lesions of the left lung were positioned as follows: 30 (58%) in the upper lobe, 8 (15%) in the lingula, and 14 (27%) in the lower lobe.

We found that 65 (49%) lesions were spicular, 54 (40%) were lobulated-contoured, and 15 (11%) had smooth and sharp edges. A hundred and twenty seven (95%) lesions were solid, while seven (5%) were cavitary.

The lesions ranged in size from 1.3 to 11 cm (median, 5 cm). The depth of the lesions from the pleura ranged from 0 to 5.5 cm (mean, 1.0

cm; median, 0.5 cm). We found that 113 (84%) lesions were peripheral, and 21 (16%) were centrally localized.

TFNA Results

The final diagnoses for the 134 cases were malignant in 122 (91%) cases and benign in the remaining 12 (9%). The TFNA biopsy results of the 134 cases were as follows: 107 (80%) malignant, 5 (4%) specific benign, and 22 (16%) nonspecific.

A hundred and sixty nine TFNA procedures were performed in the 134 cases. The diagnosis was established by TFNA in 107 of the 122 malignant lesions (88%). The cell types of the 107 malignant biopsy specimens were as follows: Adenocarcinoma in 27 (25%) cases, squamous cell in 20 (19%) cases, non-small cell carcinoma in 56 (52%) cases, small cell in 2 (2%) cases , and other in 2 (2%) cases. Each of the malignant cell types was also classified as primary or metastatic as shown in Table 1.

A specific diagnosis was achieved with TFNA in 5 of 12 benign lesions (42%). Five specific diagnoses were hamartoma in 1 (20%) case , hydatic cyst in 1 (20%) case, pneumoconiosis in 1 (20%) case, and chronic inflammation in 2 (40%) cases.

Inadequate sampling was reported in 8 (36%) of the 22 cases in which TFNA was non-specific. When all 134 cases were evaluated, the rate of inadequate sampling was 6%.

The TFNA procedure was repeated in 30 (22%) of the 134 cases, and 22 (73%) of these 30 repeated TFNA procedures were diagnostic; 8 (27%) of the cases remained nonspecific (Table 2).

Surgical and Follow-up Results

Thirty-two of 134 (24%) patients underwent surgical resection of their lung lesions. A definitive diagnosis for the lesion was obtained in all of the surgical cases. Preoperatively, 19 (59%) patients had malignant, 2 (6%) had benign, and 11 (34%) had a nonspecific diagnosis. One of the benign diagnoses was a hydatic cyst, and the other was a hamartoma. After surgical diagnosis, it was found that 23 (72%) of the lesions were malignant and 9 (28%) were benign.

Seven (78%) of these 9 cases with a TFNA diagnosis of non-small cell cancer were adenocarcinoma, and 2 (22%) were squamous cell carcinoma. When compared with the malignant TFNA diagnosis, 11 of the 19 (58%) surgical diagnoses yielded different results (Table 3). While 4 (36%)

Table 1. Results of malignant TFNAs.

Cell type	Primary	Metastatic	Total
Adenocarcinoma	21	6	27
Squamous cell	18	2	20
Small cell	2	0	2
Non-small cell	54	2	56
Others*	1	1	2

* Undifferentiated tumor.
TFNA: Transthoracic fine needle aspiration.

Table 2. Repeated TFNA results vs. final results.

Repeated TFNA results		Final results	
Malignant	19	Malignant	25
Benign	3	Benign	5
Non-specific	8	Non-specific	0

TFNA: Transthoracic fine needle aspiration.

Table 3. TFNA vs. surgical diagnosis.

TFNA diagnosis	Surgical diagnosis
1 Squamous cell	Adenocarcinoma
2 Squamous cell	Adenocarcinoma
3 Non-small cell	Adenocarcinoma
4 Non-small cell	Squamous cell
5 Non-small cell	Squamous cell
6 Non-small cell	Adenocarcinoma
7 Non-small cell	Adenocarcinoma
8 Non-small cell	Adenocarcinoma
9 Non-small cell	Adenocarcinoma
10 Non-small cell	Adenocarcinoma
11 Non-small cell	Adenocarcinoma

TFNA: Transthoracic fine needle aspiration.

of the 11 patients who had a non-specific diagnosis with TFNA obtained a malignant surgical diagnosis, 7 (64%) received a benign diagnosis.

In addition to the 11 patients who had a non-specific TFNA biopsy result and underwent thoracotomy, a diagnosis was established with mediastinoscopy in 2 patients with a non-specific TFNA result. The mediastinoscopy revealed that 1 patient had small cell cancer and the other had clear cell cancer.

In 5 cases, a pathologic diagnosis was established with other organ biopsies. In 2 of these 5 cases, chronic inflammation was seen on the TFNA pathology, and osteomyelitis was diagnosed by other biopsies (1 vertebrae biopsy, 1 rib resection). The TFNA biopsy results of the other 3 cases were nonspecific, and final pathologic diagnoses were achieved. Diagnoses were obtained in these three cases by muscle biopsy, liver biopsy, and chest wall excision biopsy, respectively. The pathologic diagnoses were malignant mesenchymal tumor metastasis, spindle cell carcinoma metastasis, and plasmacytoma.

Six cases with non-specific TFNA biopsy results were accepted as malignant based on their clinical and radiological features. In these cases, lesion progression and patient death, lesion progression and cachexia, and brain metastasis were defined as malignant criteria.

A case with a TFNA biopsy result of anthracosis was followed up for 13 months and evaluated as pneumoconiosis because the lesions remained stabile.

While definitive pathologic diagnoses were established surgically in 11 (92%) of 12 lesions, 1 (8%) was accepted as benign by clinical observation. An exact pathologic diagnosis was achieved in 116 (95%) of the 122 malignant lesions, and 6 (5%) of these cases were accepted as malignant clinically and radiologically. Table 4 shows the final pathologic diagnoses of the 22 cases with previous nonspecific TFNA biopsy results.

Table 4. Final pathologic diagnosis of 22 cases with previous nonspecific TFNA biopsy results.

Final diagnosis	n	Diagnostic method (n)
Benign lesions		
Hydatic cyst	2	Thoracotomy (2)
Tuberculosis or tuberculoma	3	Thoracotomy (3)
Pneumoconiosis	2	Thoracotomy (2)
Malignant lesions		
Adenocarcinoma	2	Thoracotomy (2)
Squamous cell carcinoma	1	Thoracotomy (1)
Small cell carcinoma	1	Mediastinoscopy (1)
Other	11	Mediastinoscopy (1), thoracotomy (1), biopsies of other sites (3), clinical-radiological malignant (6)
Total	22	

TFNA: Transthoracic fine needle aspiration.

Accuracy of TFNA

For statistical purposes, all specimens that were positive for malignancy were assumed to be true positives based on the high specificity of the TFNA technique (9,10). Cases with surgically confirmed TFNA biopsy results of a definitive benign diagnosis were assessed as true negatives. Cases with nonspecific TFNA biopsy results were assessed as false negatives. Based on these criteria, we found 107 true positives, 5 true negatives, 22 false negatives, and no false positives. Thus, the sensitivity of TFNA's for the detection of malignancy was 83%, and the overall accuracy of TFNA for diagnosing malignancy was 84%. Since no false positives occurred, the specificity for diagnosing malignancy was 100%.

Accuracy vs. Lesion Size and Localization

Table 5 gives the diagnostic accuracy and sensitivities of TFNA with respect to lesion size. The highest diagnostic accuracy and sensitivity rate was obtained for lesions that were 2.1-3.0 cm in diameter and for lesions that were bigger than 6.0 cm in diameter. No significant difference was observed among groups with respect to the diagnostic accuracy or sensitivity rates.

Table 5. Sensitivity and diagnostic accuracy of TFNA with respect to lesion size*.

Size (cm)	Malignant (n)	Benign (n)	Nonspecific (n)	Total (n)	Accuracy (%)	Sensitivity (%)
1.0-2.0	3	1	1	5	80	75
2.1-3.0	17	0	2	19	89	89
3.1-4.0	17	2	4	23	83	81
4.1-5.0	25	2	9	36	75	74
5.1-6.0	10	0	2	12	83	83
> 6.0	35	0	4	39	90	90

* p> 0.05

TFNA: Transthoracic fine needle aspiration.

In centrally located lesions, we found that the diagnostic accuracy was 71% and the sensitivity was 71%. In peripheral lesions, we found that the diagnostic accuracy was 86% and the sensitivity was 85%. Although accuracy and sensitivity were lower in centrally located lesions, no significant statistics were observed.

Complications of TFNA

The most commonly encountered complication after TFNA was pneumothorax in this series. Pneumothorax occurred in 22 of the 134 (16%) patients. Of these 22 patients, 7 (32%) required chest tube placement because the size of the pneumothorax was 20% or greater. The total incidence of pneumothorax requiring a chest tube was 5%.

Pneumothorax was more frequently observed in centrally located lesions. It was detected in 9 (43%) of the 21 centrally located lesions and in 13 (12%) of the 113 peripheral lesions (p= 0.001).

While the lesion depth was 1.9 ± 1.1 cm (min 0.2, max 4.3 cm) in the pneumothorax group, it was 0.6 ± 1.1 cm (min 0.0, max 5.5 cm) in the nonpneumothorax group. The difference was statistically significant (p= 0.001).

Table 6. Lesion size and pneumothorax frequency in peripheral lesions.

Size of lesion (cm)	n	Pneumothorax frequency n (%)
1.0-3.0	18	5 (28)*
3.1-5.0	45	6 (13)
> 5.1	50	2 (4)

* p= 0.022

In centrally located lesions, no significant differences were observed between the lesion size and pneumothorax occurrence rate. In peripheral lesions, 28% of the subjects with lesions of 1.0 to 3.0 cm in size developed pneumothorax, which was a statistically significant rate of occurrence (p= 0.022) (Table 6).

The only additional complication encountered other than pneumothorax in the 134 cases was 7 (5%) cases of minimal parenchymal hemorrhage. All of these were minor, self-resolving complications that did not require any clinical intervention.

DISCUSSION

TFNA biopsy is known to be a reliable and successful diagnostic tool. Our study also confirmed that it is a powerful diagnostic tool especially for malignant pulmonary lesions. Diagnoses were achieved with TFNA in 107 (88%) of 122 malignant pulmonary lesions. In the last 10 years, it has been reported that the sensitivity of TFNA biopsy in malignant lesion diagnosis is 74-95% (1,8,11-15). The sensitivity rate in our study was 83%, which is in the range found in the literature, but is closer to the lower limit probably because we accepted all nonspecific TFNA biopsy results as false negatives for the purpose of statistical evaluation. If we consider only the 122 malignant lesions, our sensitivity rate rises to 88%.

Despite the high sensitivity of TFNA biopsy in malignant pulmonary lesions, low diagnostic rates have been reported in benign pulmonary lesions. The rate of obtaining a benign definitive diagnosis with TFNA biopsy is 20-48% (6,8,12,13,16,17). Our definitive benign diagnosis rate was high at 42%. In benign pulmonary lesions, cutting needle biopsy has a higher diagnostic ability when compared to TFNA. Although it is not advantageous in malignant lesion diagnosis, definitive benign diagnosis rates are 69-92% with cutting needle biopsy (4,6,16-18). Boiselle et al. reported that cutting needle biopsy plus TFNA raised the rate of diagnosis significantly in benign lesions (6).

Several factors can lead to non-specific TFNA biopsy results. The most common factors are tumor necrosis, inappropriate biopsy, and insufficient sampling (19). The non-specific biopsy rates were 25% in a series of 130 cases by Larscheid et al. and 18% in 294 cases by Arslan et al. our rate was 16% our insufficient sampling rate was 6%, which was responsible for 36% of the non-specific biopsy rates (11,12).

Histopathologic biopsy results have been reported to be more reliable than cytological evaluation when determining the cell type of malignant lesions with TFNA biopsy (20,21). In contrast, studies have reported that cytological differentiation could be made properly in small cell and non-small cell lung cancers (11,22). In a 130-case series by Larscheid et al. minor differences in cell types were detected in only four non-small cell cancers. Furthermore, they reported no differences between small and non-small cell types (11). We also did not observe a cytological sorting error in small and non-small cell cancers. The differences seen in non-small cell cancers were defined as clinically unimportant.

A few studies have reported that lesion size affects the diagnostic success of TFNA. Larscheid et al. reported that the sensitivity and diagnostic accuracy were 67% and 70% in small tumors (< 3 cm) but 81% and 82% in big tumors (≥ 3 cm), respectively, but they could not find a significant difference (11). Li et al. reported that the diagnostic accuracy was 74% in non-small tumors (≤ 1.5 cm) and 96% in big tumors (> 1.5 cm) with a significant difference (23). In the study by Layfield et al., CT and fluoroscopy-guided TFNA revealed that the sensitivity was 84% in small tumors (≤ 2 cm) and 93% in big tumors (> 2 cm) with no significant difference (1). Arslan et al. found no statistical difference between tumor size and sensitivity (12). Our study also revealed no significant difference between lesion size and diagnostic accuracy and sensitivity.

The location of the tumor is another factor affecting the TFNA biopsy results. In our series, TFNA applied to centrally located lesions had a lower diagnostic accuracy and sensitivity compared to peripheral lesions with no statistical significance. Similarly, Arslan et al. reported no significant difference in the sensitivity in either location (12). However, Layfield et al. reported that the sensitivity was 100% in peripheral lesions and 82% in central lesions with a significant difference (1).

All TFNA biopsies in our series were performed using a single-pass needle. The biopsy procedure was repeated in 30 (22%) of the 134 cases. We thought that this rate was high because no on-site pathological evaluation was made. In a study comparing the single-pass needle technique with a multiple-pass coaxial needle system, no significant differences were seen between the rates of diagnostic accuracy and complications of both techniques with an emphasis on the low expense of a single-pass needle. The same study showed that doing an on-site pathologic evaluation during the biopsy procedure decreased the rate of insufficient sampling and increased the diagnostic accuracy of the procedure (24).

The most common complication of TFNA biopsy is pneumothorax. The pneumothorax rate reported over the last 10 years was 8-45%, but most of the rates were above 20% (4,6,8,11,12,14-16,18,23,25,26). In our series, the rate was 16%, and only 7 cases required chest tube placement. We speculate that 2 main reasons were responsible for this low rate of pneumothorax. The first likely reason was the choice to perform a single pass through the least ae-

rated section of lung during biopsy, avoiding bullae and fissures. The second likely reason was that the lesions were located on the pleura in 75 (56%) of our cases, which made it unnecessary to pass through aerated lung tissue. When evaluating the pneumothorax frequency according to lesion location, centrally located lesions caused significantly more instances of pneumothorax. Kazerooni et al. showed that an increased lesion depth and small lesion size were strongly correlated with pneumothorax development (25). In our series, the parenchyma depth traversed for sampling was deeper in cases that developed pneumothorax. While no significant differences were observed between the lesion size and pneumothorax occurrence rate in centrally located lesions, pneumothorax developed frequently in peripheral lesions of 1.0 to 3.0 cm. The only complication other than pneumothorax was self-resolving, clinically unimportant, minimal parenchymal hemorrhage in 7 (5%) cases.

In conclusion, our results suggest that CT-guided TFNA has a high diagnostic accuracy and low rates of complication, especially in malignant lesions, even under conditions with no possibility of on-site pathologic evaluation. CT-guided TFNA will reduce the need for invasive techniques like mediastinoscopy, video-assisted thoracoscopy, and diagnostic thoracotomy in the diagnosis of pulmonary lesions. Moreover, we suggest that the most important factor increasing the risk of pneumothorax is an increase in the depth of aerated lung traversed for sampling.

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